Unit 3
Cell Metabolism

Chapter 6: An Introduction to Metabolism

An organism's metabolism transforms matter and energy

- **Catabolic pathways =**
  - Release energy by breaking down complex molecules into simpler compounds
  - Ex: Hydrolysis, digestion, cellular respiration
- **Anabolic pathways =**
  - Consume energy to build complex molecules from simpler ones
  - Ex: Dehydration reactions (such as synthesis of protein from amino acids)

The Laws of Thermodynamics

- **First law of thermodynamics**
  - Energy can be transferred and transformed, but it cannot be created or destroyed
  - IE: Conservation of energy
- **Second law of thermodynamics**
  - Every energy transfer or transformation increases the entropy of the universe
  - **Entropy** is a measure of disorder, or randomness

- **Spontaneous processes** occur without energy input
  - Can happen quickly or slowly
  - "Energetically favorable"
- For a process to occur without energy input, it must increase the entropy of the universe!

- Catabolic reactions increase entropy
- Anabolic reactions decrease entropy
  - Must put in energy!

Gibbs Free Energy

- **Free energy** = energy that can do work

$$\Delta G = \Delta H - T\Delta S \qquad \Delta G = G_{\text{final state}} - G_{\text{initial state}}$$

- ΔH = change in the system's enthalpy (heat)
- ΔS = change in the system's entropy (disorder)
- T = absolute temperature in K (K = ℃ + 273)

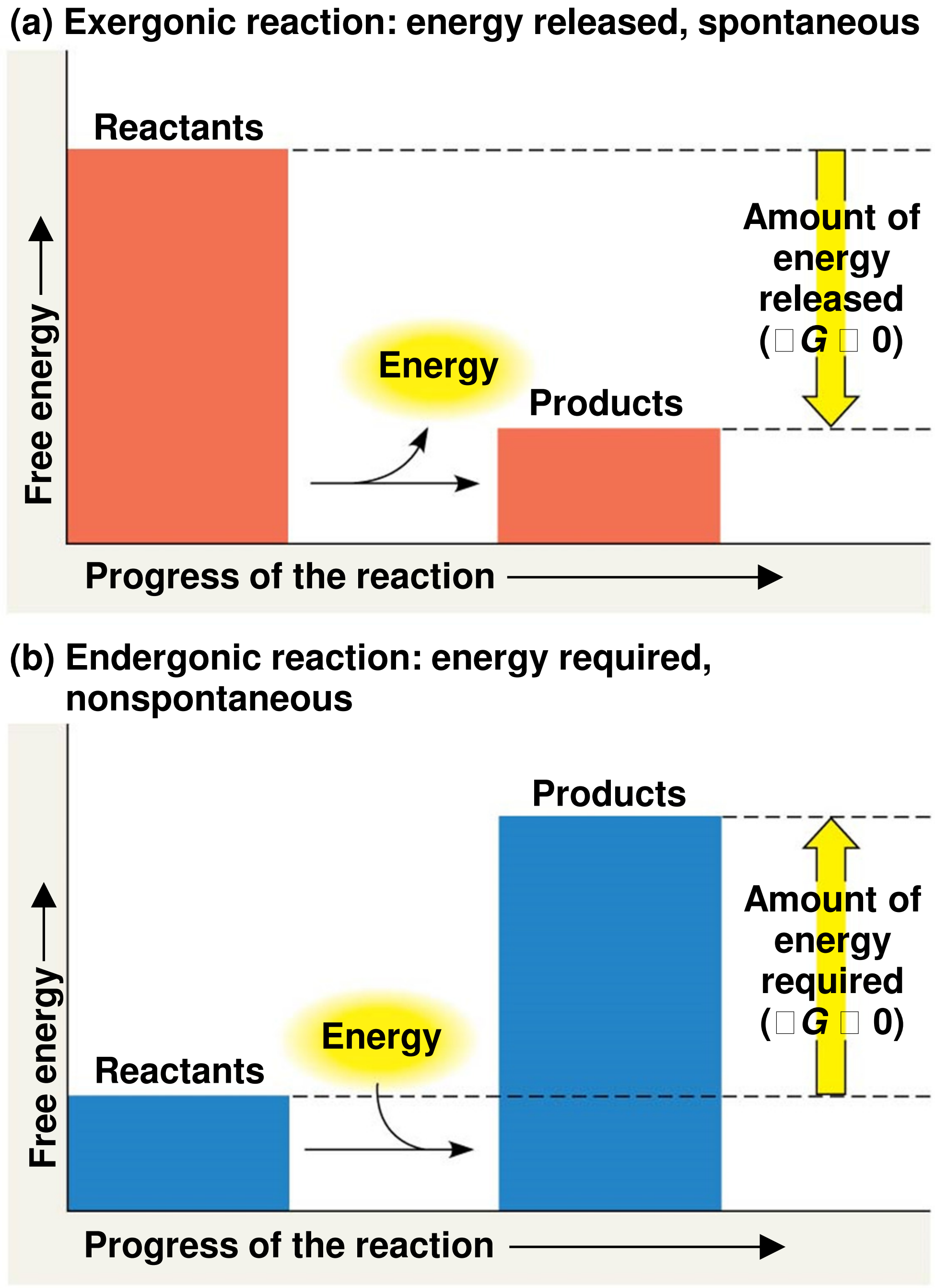
- Exothermic reactions release heat energy
- Endothermic reactions absorb heat energy

- ΔG can be used to predict if a process is energetically favorable
  - Only processes with a negative ΔG are spontaneous!
    - IE-No input of energy needed
    - Spontaneous processes can be harnessed to perform work

- An **exergonic reaction** proceeds with a net release of free energy
  - ΔG is negative
  - Spontaneous (energetically favorable)
  - Ex: respiration
- The magnitude of ΔG represents the maximum amount of work the reaction can perform

- An **endergonic reaction** absorbs free energy from its surroundings
  - ΔG is positive
  - Nonspontaneous
  - Ex: photosynthesis
- The magnitude of ΔG is the quantity of energy required to drive the reaction

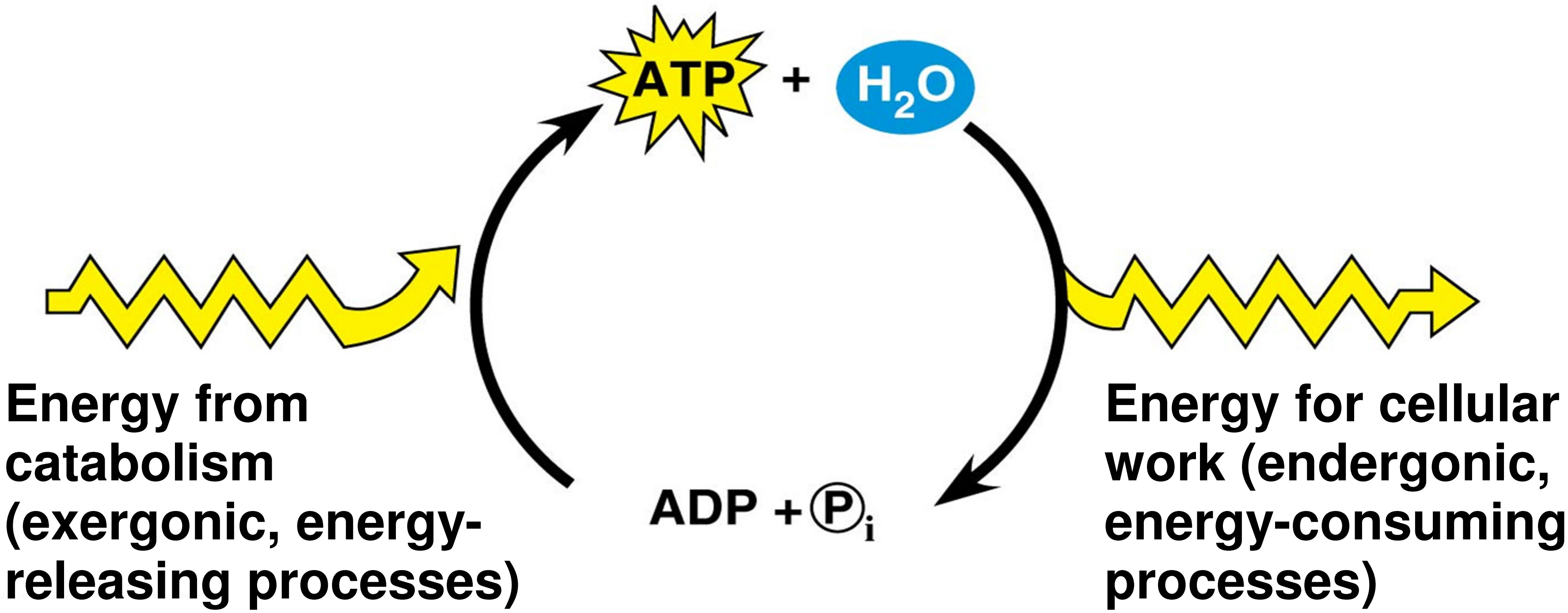
Figure 6.6


(a) Exergonic reaction: energy released, spontaneous
Reactants
Energy
Products
Amount of energy released (□G □ 0)
Free energy
Progress of the reaction
(b) Endergonic reaction: energy required, nonspontaneous
Products
Energy
Reactants
Amount of energy required (□G □ 0)
Free energy
Progress of the reaction

ATP

- To do work, cells manage energy resources by **energy coupling**
  - The use of an exergonic process to drive an endergonic one
- Most energy coupling in cells is mediated by ATP
- The bonds between the phosphate groups of ATP can be broken by hydrolysis
- Energy is released from ATP when the terminal phosphate bond is broken
  - Exergonic

- ATP drives endergonic reactions by *phosphorylation*
  - Transferring a phosphate group to some other molecule
- ATP is renewable, as it can be regenerated by addition of a phosphate group to adenosine diphosphate (ADP)

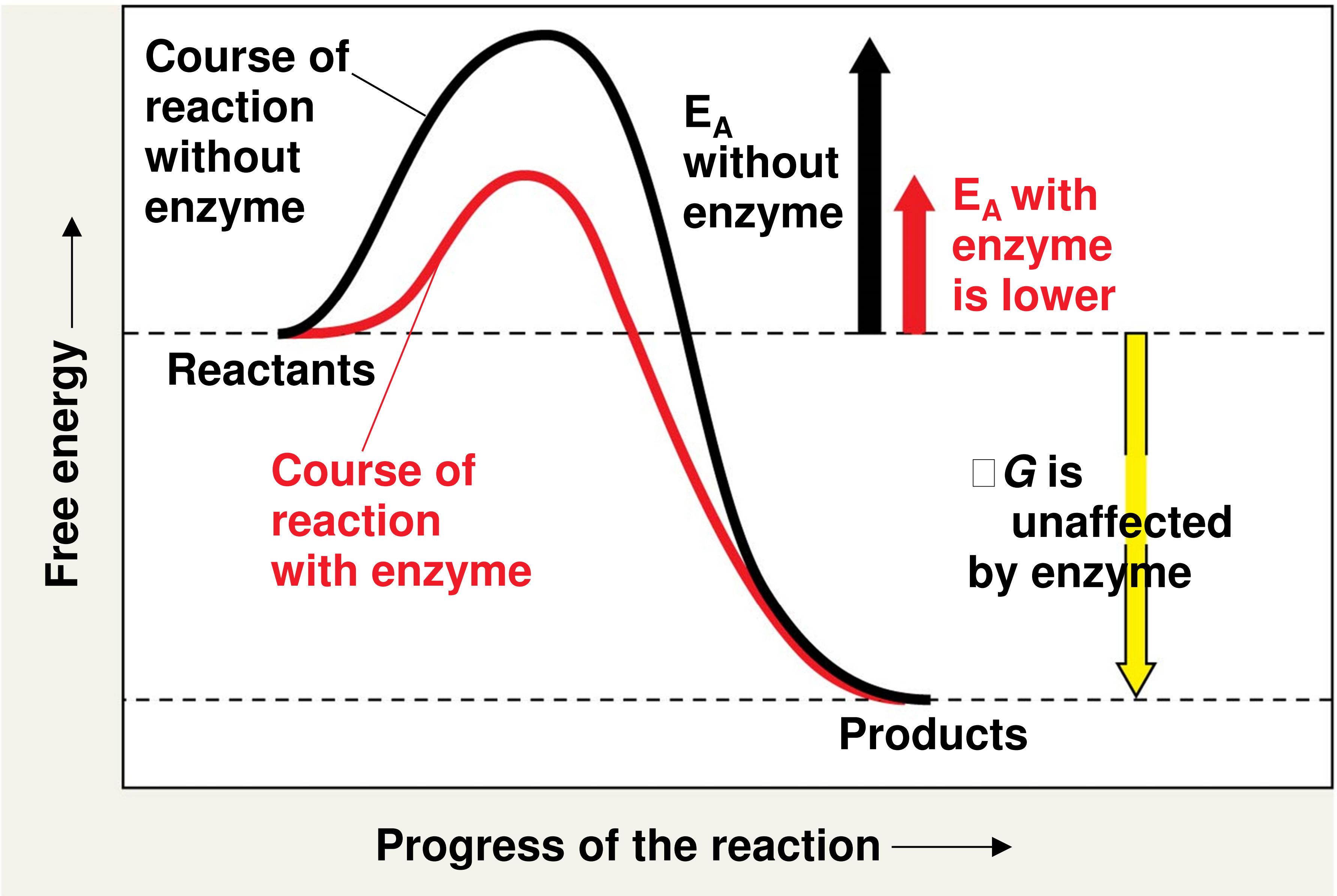


Enzymes

- A **catalyst** is a chemical agent that
  - Speeds up a reaction
  - Without being consumed by the reaction
- An **enzyme** is a catalytic protein
- The initial energy needed to start a chemical reaction is called the **activation energy**

- Enzymes catalyze reactions by lowering the activation energy barrier
- Enzymes do not affect the change in free energy (ΔG)!
  - Cannot make an endergonic reaction exergonic!
  - Instead, they hasten reactions that would occur eventually
- Enzymes are very <u>specific</u> for the reactions they catalyze based on their <u>shape</u>
- Enzymes can be used over and over again because they emerge from the reaction in their original form

Figure 6.13


Course of reaction without enzyme
E_A without enzyme
E_A with enzyme is lower
Reactants
Course of reaction with enzyme
ΔG is unaffected by enzyme
Products
Free energy
Progress of the reaction

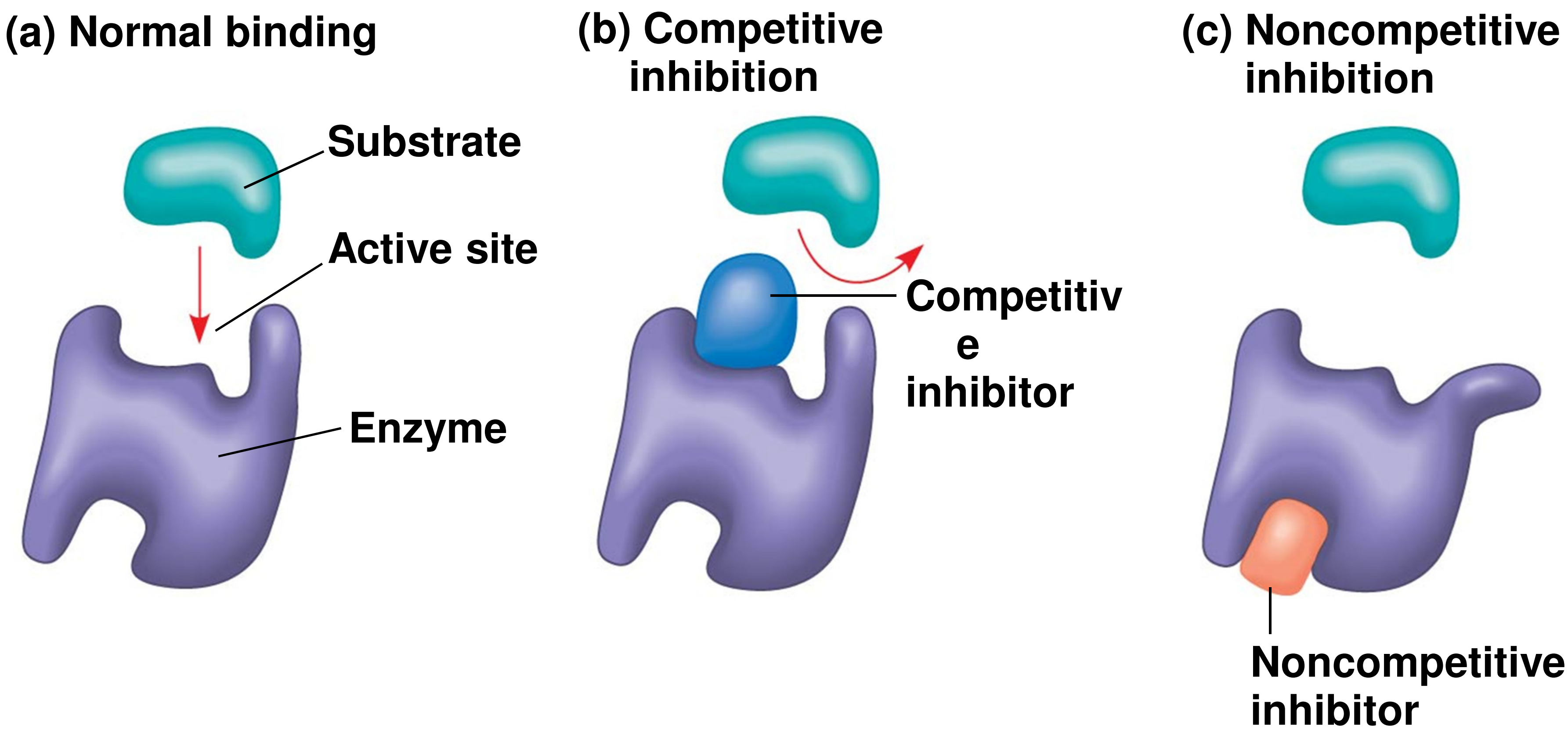
- An enzyme's activity can be affected by
  - Temperature
  - pH
  - Chemicals that specifically influence the enzyme

- **Cofactors** are nonprotein enzyme helpers
  - An organic cofactor is called a **coenzyme**

Enzyme Inhibitors

- **Competitive inhibitors** mimic the normal substrate and bind to the active site of an enzyme
  - Block substrates from entering active sites, competing with the substrate
  - Can be overcome by increasing concentration of substrate
- **Noncompetitive inhibitors** bind to another part of an enzyme, causing the enzyme to change <u>shape</u> and making the active site less effective
  - Do not directly compete with substrate

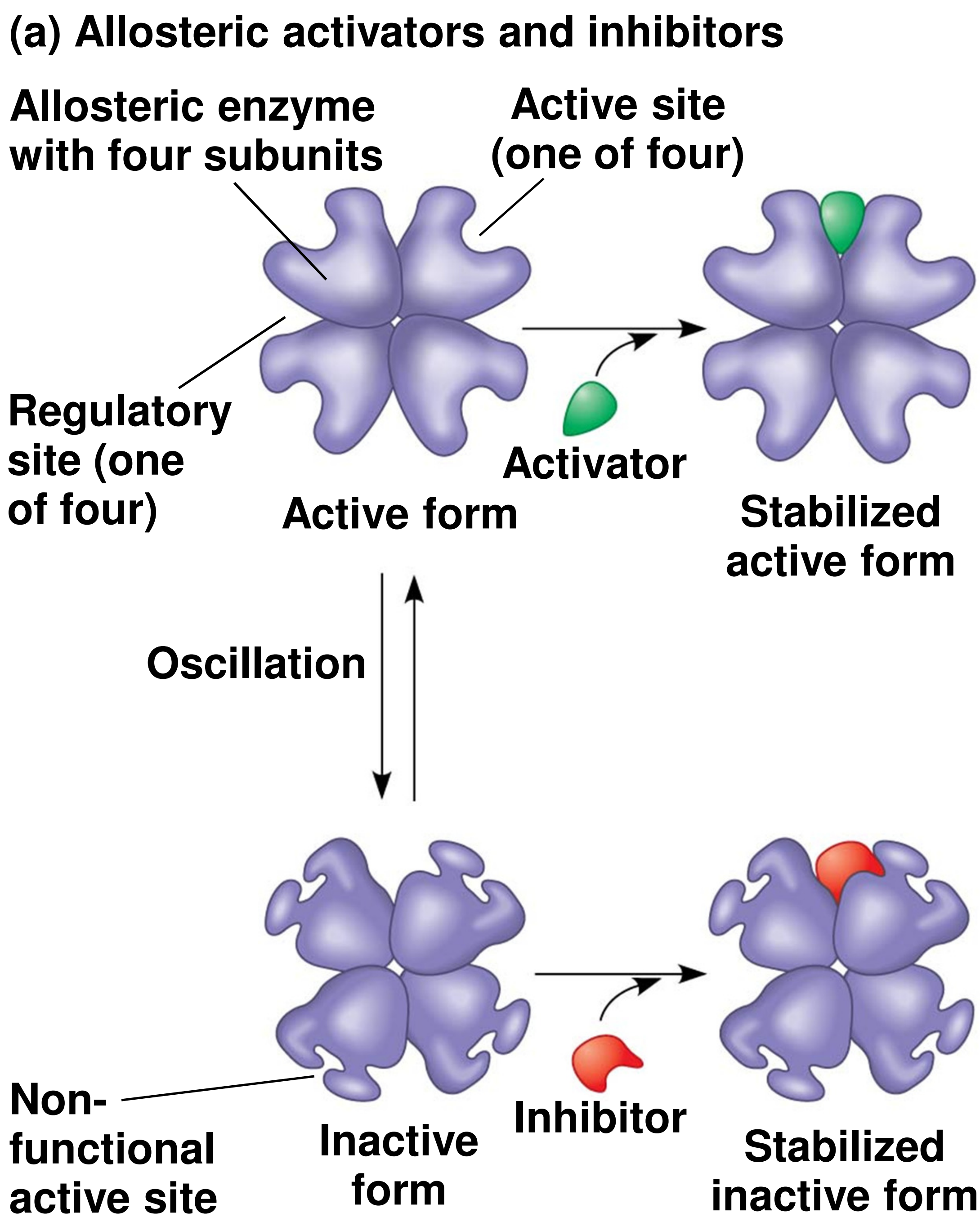
Figure 6.17


(a) Normal binding
Substrate
Active site
Enzyme
(b) Competitive inhibition
Competitiv
e
inhibitor
(c) Noncompetitive inhibition
Noncompetitive
inhibitor

Regulation of Enzymes

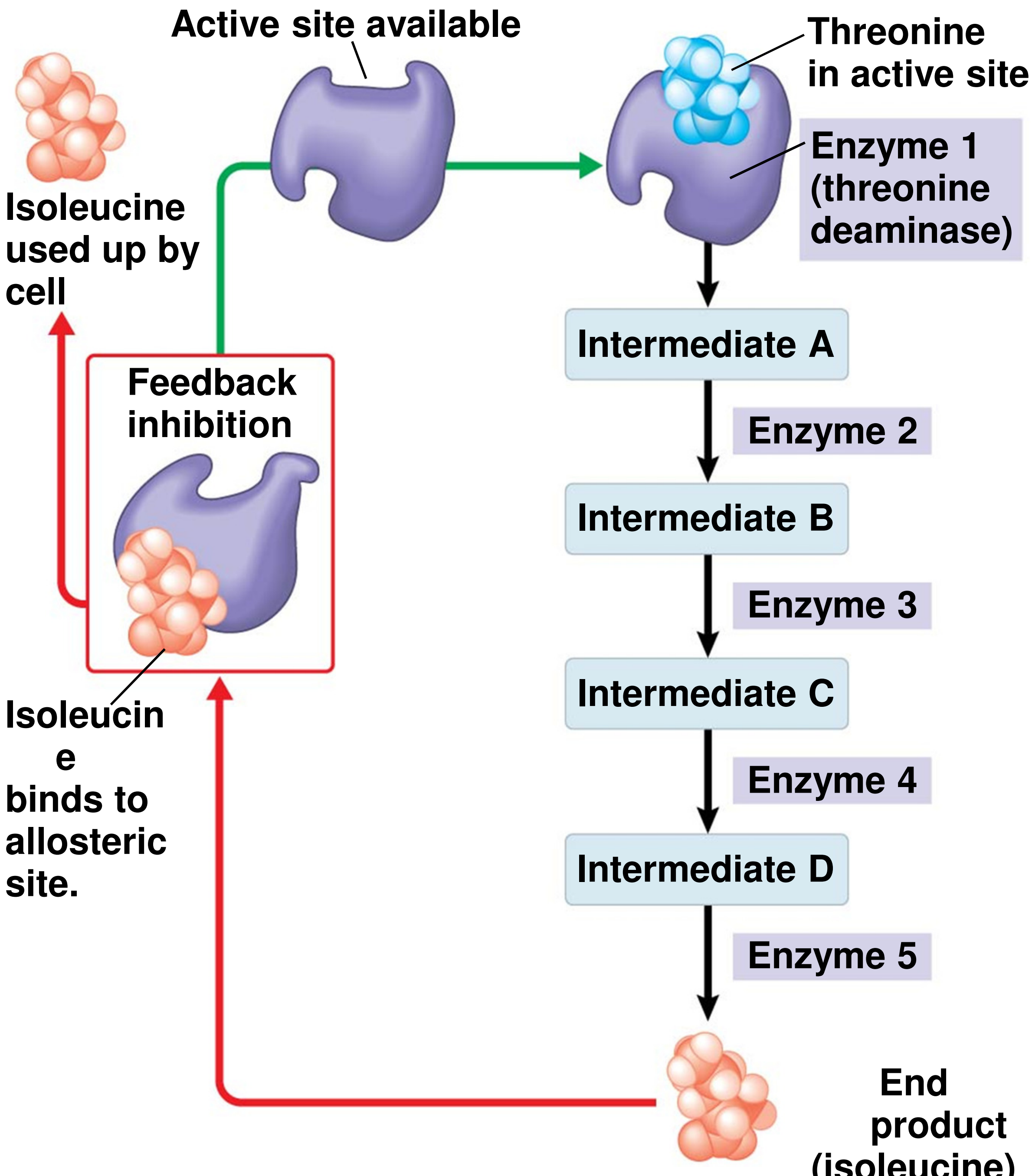
- Regulatory molecules change an enzyme's shape and the functioning of its active site
  - Bind elsewhere on enzyme
  - Similar to reversible noncompetitive inhibitors
- **Allosteric regulation =**
  - Regulatory molecule binds to a protein at one site and affects the protein's function at another site
    - The binding of an *activator* stabilizes the active form of the enzyme
    - The binding of an *inhibitor* stabilizes the inactive form of the enzyme

Figure 6.18a


(a) Allosteric activators and inhibitors
Allosteric enzyme with four subunits
Active site (one of four)
Regulatory site (one of four)
Active form
Activator
Stabilized active form
Oscillation
Non-functional active site
Inactive form
Inhibitor
Stabilized inactive form

- **Cooperativity** is a form of allosteric regulation
  - A substrate binds to one active site, triggering a shape change that facilitates binding of additional substrates
  - Can amplify enzyme activity
- In **feedback inhibition**, the end product of a metabolic pathway shuts down the pathway
  - Prevents a cell from wasting chemical resources by synthesizing more product than is needed

Figure 6.19


Active site available
Threonine in active site
Enzyme 1 (threonine deaminase)
Isoleucine used up by cell
Feedback inhibition
Intermediate A
Enzyme 2
Intermediate B
Enzyme 3
Intermediate C
Enzyme 4
Intermediate D
Enzyme 5
Isoleucin e binds to allosteric site.
End product (isoleucine)

Unit 3
Cell Metabolism

Chapter 7: Cellular Respiration and Fermentation

Energy Conversion Overview

- Energy flows into an ecosystem as sunlight and leaves as heat
  - Energy flows in a one-way direction
  - In contrast, the chemical elements essential to life are recycled
- Photosynthesis generates O_2 and organic molecules, which are used as fuel for cellular respiration
- Respiration uses chemical energy stored in organic molecules to regenerate ATP, which powers work

Catabolic pathways

- The breakdown of organic molecules is exergonic
  - Some of the energy can be used to do work
  - Some is dissipated as heat
- **Fermentation** is a partial degradation of sugars that occurs without O_2
- **Aerobic respiration** consumes organic molecules and O_2 and yields ATP
  - Most efficient
- Anaerobic respiration is similar to aerobic respiration but consumes compounds other than O_2

The Stages of Cellular Respiration Overview

- Harvesting of energy from glucose has three stages

1. **Glycolysis**
   - Breaks down glucose into two molecules of pyruvate
   - Occurs in cytosol
   - Glycolysis occurs whether or not O_2 is present!
2. Pyruvate oxidation and the **citric acid cycle**
   - Completes the breakdown of glucose to carbon dioxide
   - Occurs in mitochondria of eukaryotes

3. **Oxidative phosphorylation**

- Electron transport and chemiosmosis
  - Accounts for most of the ATP synthesis
  - Note: A smaller amount of ATP is formed in glycolysis and the citric acid cycle by **substrate-level phosphorylation**

Flow of electrons

- Glucose → NADH → electron transport chain → oxygen

Glycolysis

- Glycolysis ("sugar splitting") breaks down glucose into two molecules of pyruvate
- Occurs in the cytoplasm
- Has two major phases
  - Energy investment phase
    - 2 ATP used
  - Energy payoff phase
    - 4 ATP formed (2 net ATP produced)
    - 2 NADH result (electron carriers)
- Glycolysis occurs whether or not O_2 is present!

Citric Acid Cycle (AKA Krebs Cycle)

- If O_2 is present, pyruvate enters the mitochondrion
- The citric acid cycle, also called the *Krebs cycle*, completes the breakdown of pyruvate to CO_2
  - Thus CO_2 is a waste product of respiration!
- After 2 turns, the citric acid cycle generates
  - 2 ATP (substrate level phosphorylation)
  - 6 NADH (electron carrier)
  - 2 $FADH_2$ (electron carrier)

Oxidative phosphorylation (ETC and Chemiosmosis)

- So far only 4 ATP molecules per glucose molecule were produced by substrate-level phosphorylation
  - 2 net ATP from glycolysis
  - 2 ATP from citric acid cycle
- NADH and $FADH_2$ account for most of the energy extracted from food
  - These electron carriers donate electrons to the electron transport chain, which powers ATP synthesis via oxidative phosphorylation

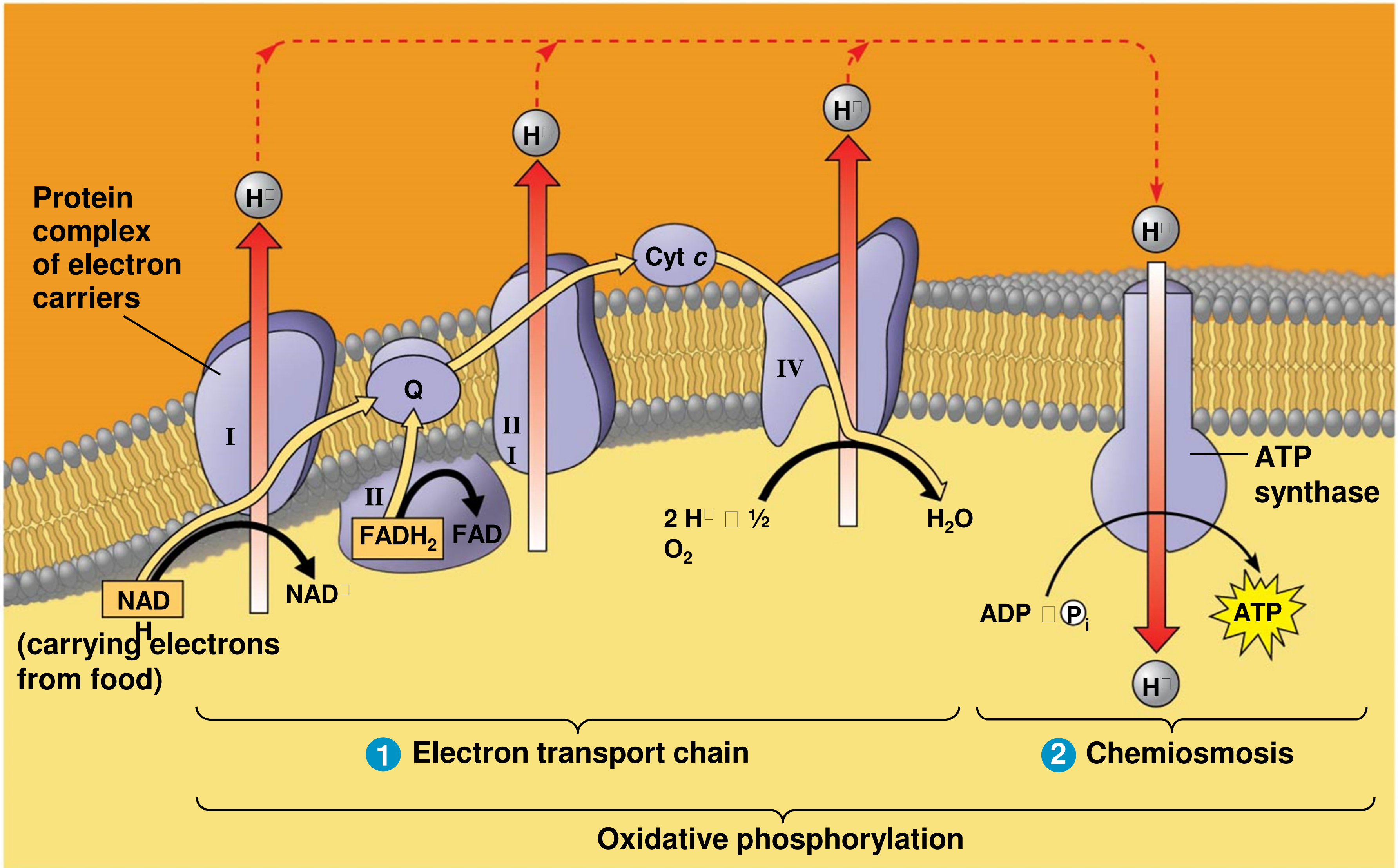
Electron Transport Chain

- ETC is in the inner membrane of the mitochondrion
  - Folding of membrane to form cristae increases surface area
  - More space for more chains!
- Electrons are transferred from NADH or $FADH_2$ to the electron transport chain
  - Oxygen is the final electron acceptor (aerobic!)
  - The ETC generates no ATP directly
  - It breaks the large free-energy drop from food to O_2 into smaller steps that release energy in manageable amounts

Chemiosmosis

- Proton gradient established from electron transport chain causes proteins to pump H^+ from the mitochondrial matrix to the intermembrane space
- H^+ then moves back across the membrane, passing through the protein complex, **ATP synthase**
  - Uses the exergonic flow of H^+ to drive phosphorylation of ATP
    - IE-ATP synthase makes ATP from ADP and inorganic phosphate
- This is an example of **chemiosmosis**, the use of energy in a H^+ gradient to drive cellular work

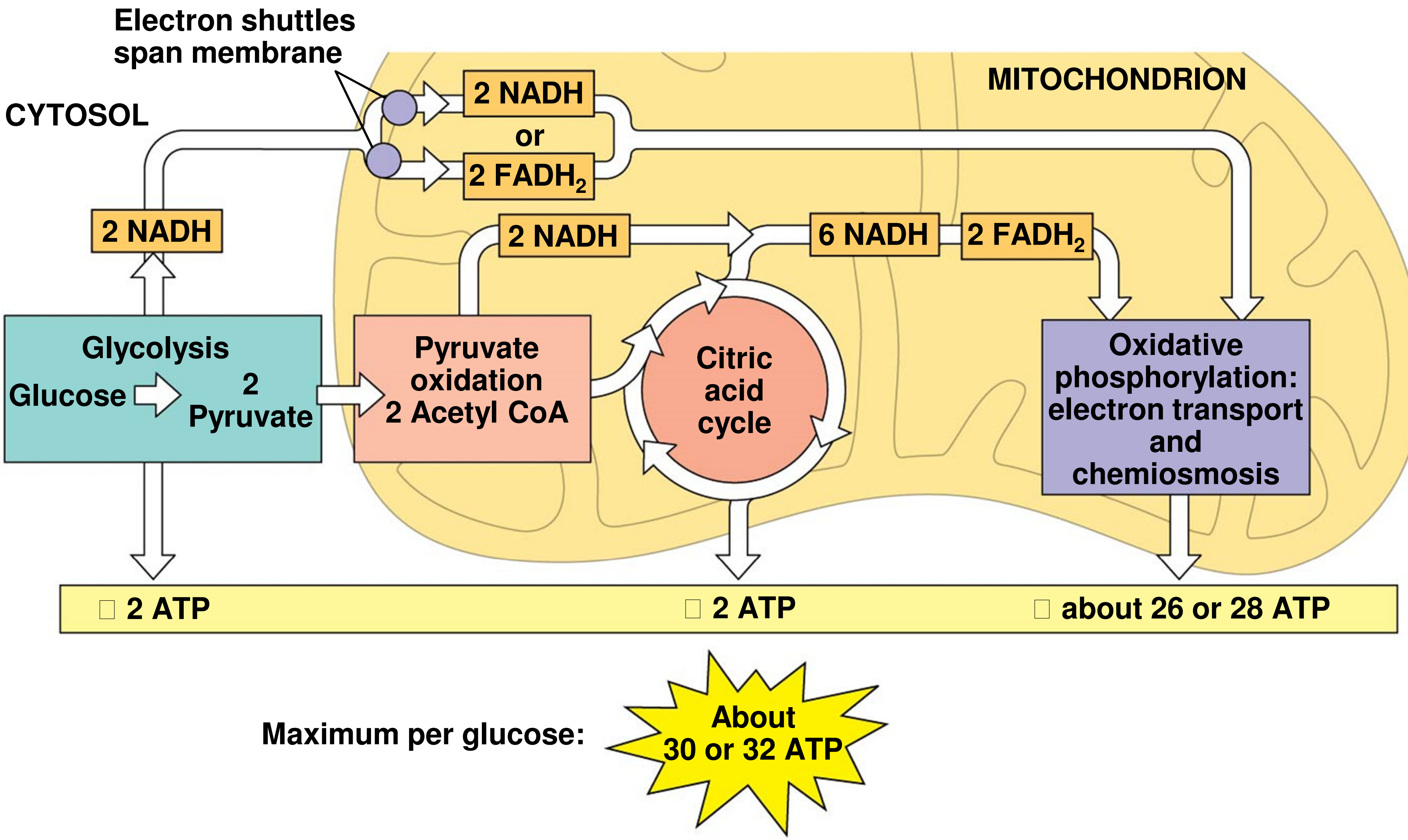
Figure 7.14


Protein complex of electron carriers
H
H
H
H
H
I
Q
II I
Cyt c
IV
II
FADH2
FAD
NAD H
NAD
(carrying electrons from food)
2 H ½ O2
H2O
ATP synthase
ADP P i
ATP
1 Electron transport chain
2 Chemiosmosis
Oxidative phosphorylation

Energy Flow in Cellular Respiration

- During cellular respiration, most energy flows in the following sequence:
  - Glucose
  - NADH
  - Electron transport chain (O_2 at end)
  - Proton-motive force
  - ATP
- Total yield of about 32 ATP during respiration
  - Also produces six molecules of CO_2

Figure 7.15

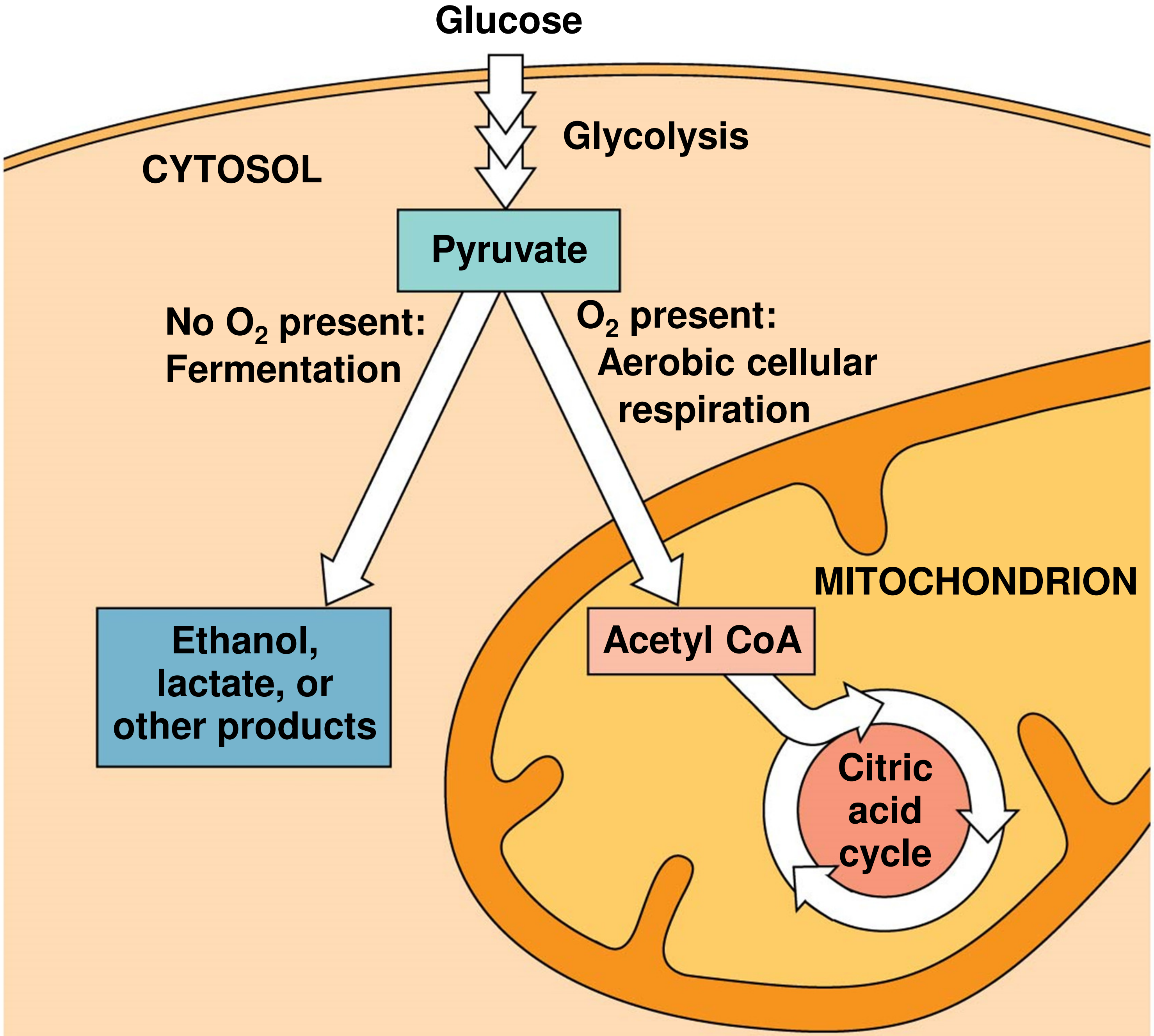

Electron shuttles span membrane
CYTOSOL
MITOCHONDRION
2 NADH
or
2 FADH$_2$
2 NADH
2 NADH
6 NADH
2 FADH$_2$
Glycolysis
Glucose
2 Pyruvate
Pyruvate oxidation
2 Acetyl CoA
Citric acid cycle
Oxidative phosphorylation: electron transport and chemiosmosis
 2 ATP
 2 ATP
 about 26 or 28 ATP
Maximum per glucose:
About 30 or 32 ATP

Fermentation

- No O_2 = No electron transport chain
- In that case, glycolysis couples with fermentation or anaerobic respiration to produce ATP

- **Obligate anaerobes** carry out only fermentation or anaerobic respiration
  - Cannot survive in the presence of O_2!
- Yeast and many bacteria are **facultative anaerobes**
  - They can survive using either fermentation or cellular respiration

Figure 7.17


Glucose
Glycolysis
CYTOSOL
Pyruvate
No O_2 present:
Fermentation
O_2 present:
Aerobic cellular
respiration
MITOCHONDRION
Ethanol,
lactate, or
other products
Acetyl CoA
Citric
acid
cycle

- **Alcoholic fermentation**
  - Pyruvate is converted to ethanol
  - Also releases CO_2
  - Used by yeast in brewing, winemaking, and baking
- **Lactic acid fermentation**
  - Pyruvate is reduced by NADH, forming <u>lactate</u> as an end product
  - NO release of CO_2!
  - Used by some fungi and bacteria to make cheese and yogurt
  - Used by human muscle cells fermentation to generate ATP when O_2 is scarce (exercise)

Comparing Fermentation and Respiration

- Similarities
  - All use glycolysis to oxidize glucose
    - (2 net ATP)
  - NAD^+ is the oxidizing agent that accepts electrons during glycolysis
- Differences
  - Different final electron acceptor
  - Different amounts of ATP produced
    - Respiration harvests much more energy!

Unit 3
Cell Metabolism
Chapter 8: Photosynthesis

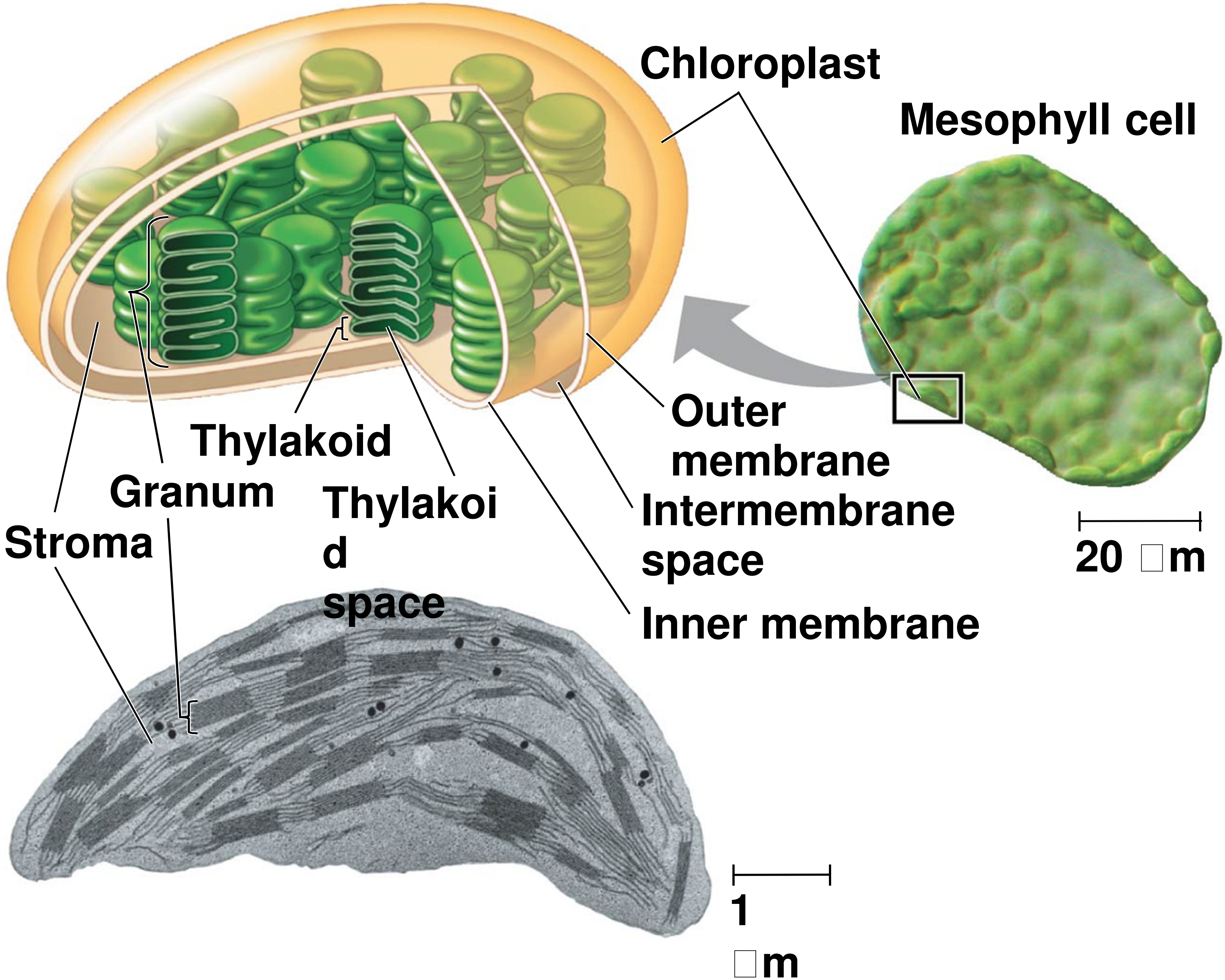
Photosynthesis: Energy Conversion

- **Photosynthesis** is the process that converts solar energy into chemical energy
- $6\ CO_2 + 12\ H_2O + \text{Light energy} \rightarrow C_6H_{12}O_6 + 6\ O_2 + 6\ H_2O$
- Overall chemical change during photosynthesis is the reverse of that during cellular respiration
- Occurs in plants, algae, certain other protists, and some prokaryotes
- Photosynthesis is an <u>endergonic</u> process
  - Requires input of energy
    - Provided by light

Chloroplasts

- Leaves are the major locations of photosynthesis
- Their green color is from **chlorophyll**, the green pigment within chloroplasts
- Chloroplasts are found mainly in cells of the **mesophyll**, the interior tissue of the leaf
- CO_2 enters and O_2 exits the leaf through microscopic pores called **stomata**
- Water and sugar are transported through veins
- The chlorophyll is in the membranes of **thylakoids** (connected sacs in the chloroplast)
  - Thylakoids may be stacked in columns called *grana*
- Chloroplasts also contain **stroma**, a dense interior fluid

Figure 8.3b

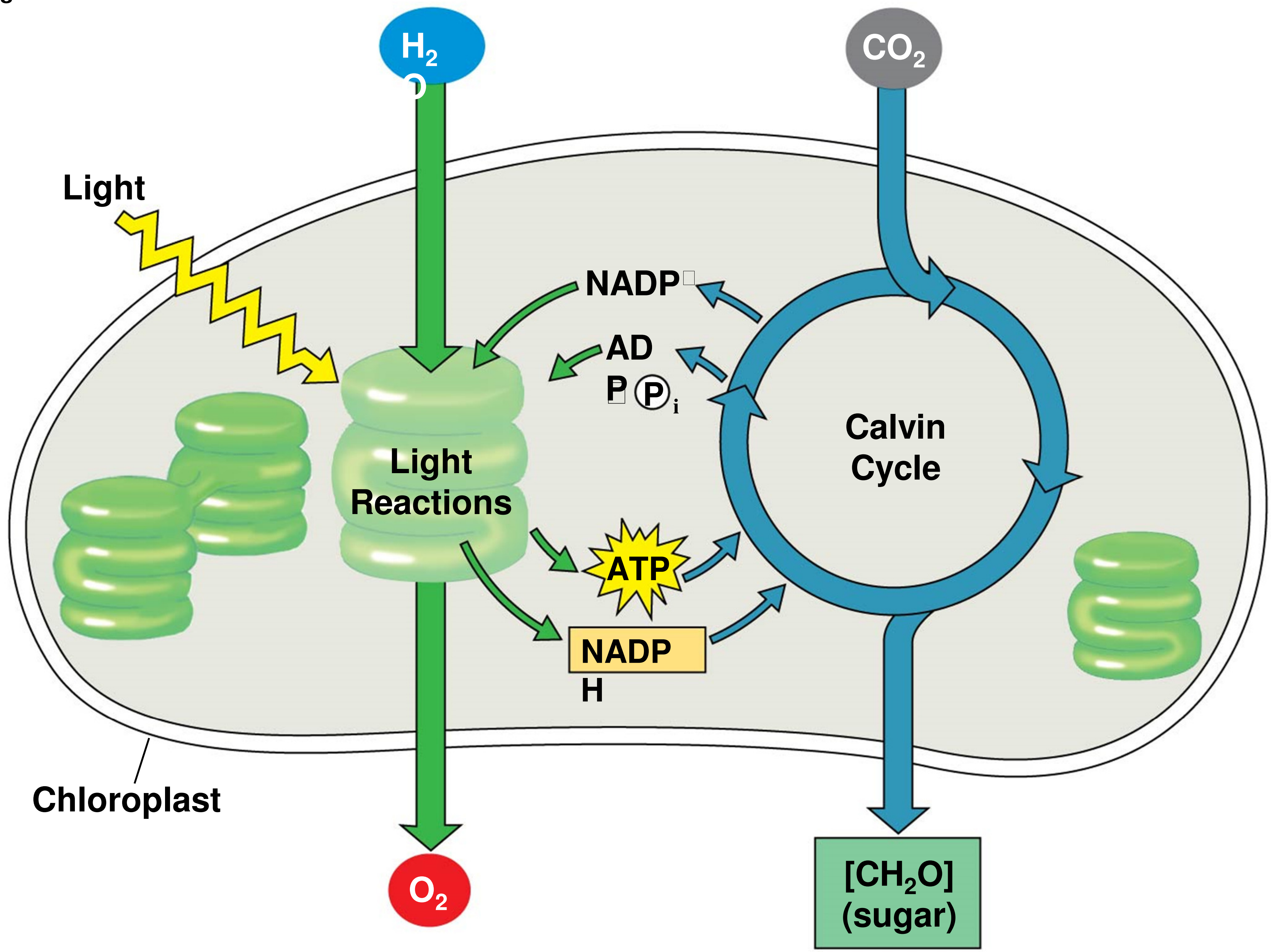

Chloroplast
Mesophyll cell
Outer membrane
Intermembrane space
Inner membrane
Thylakoid
Granum
Thylakoid space
Stroma
20 □m
1 □m

Two Stages of Photosynthesis Overview

- Photosynthesis consists of two stages:
  - **Light reactions** (the *photo* part)
  - **Calvin cycle** (the *synthesis* part)
- The light reactions (in the thylakoids)
  - Split H_2O
    - Provides source of electrons and protons (H^+)
  - Release O_2 as byproduct
  - Reduce the electron acceptor, **$NADP^+$**, to NADPH
  - Generate ATP from ADP by adding a phosphate group, **photophosphorylation**

- The Calvin cycle (in the stroma)
  - Forms sugar from CO_2, using ATP and NADPH
  - Begins with **carbon fixation**
    - Incorporating CO_2 into organic molecules
  - Sometimes called light-independent reactions
    - Does not need light DIRECTLY
    - But relies on ATP produced from light reactions

Figure 8.5-4


H2
O
CO2
Light
NADP
AD
P
P i
Calvin
Cycle
Light
Reactions
ATP
NADP
H
Chloroplast
O2
[CH2O]
(sugar)

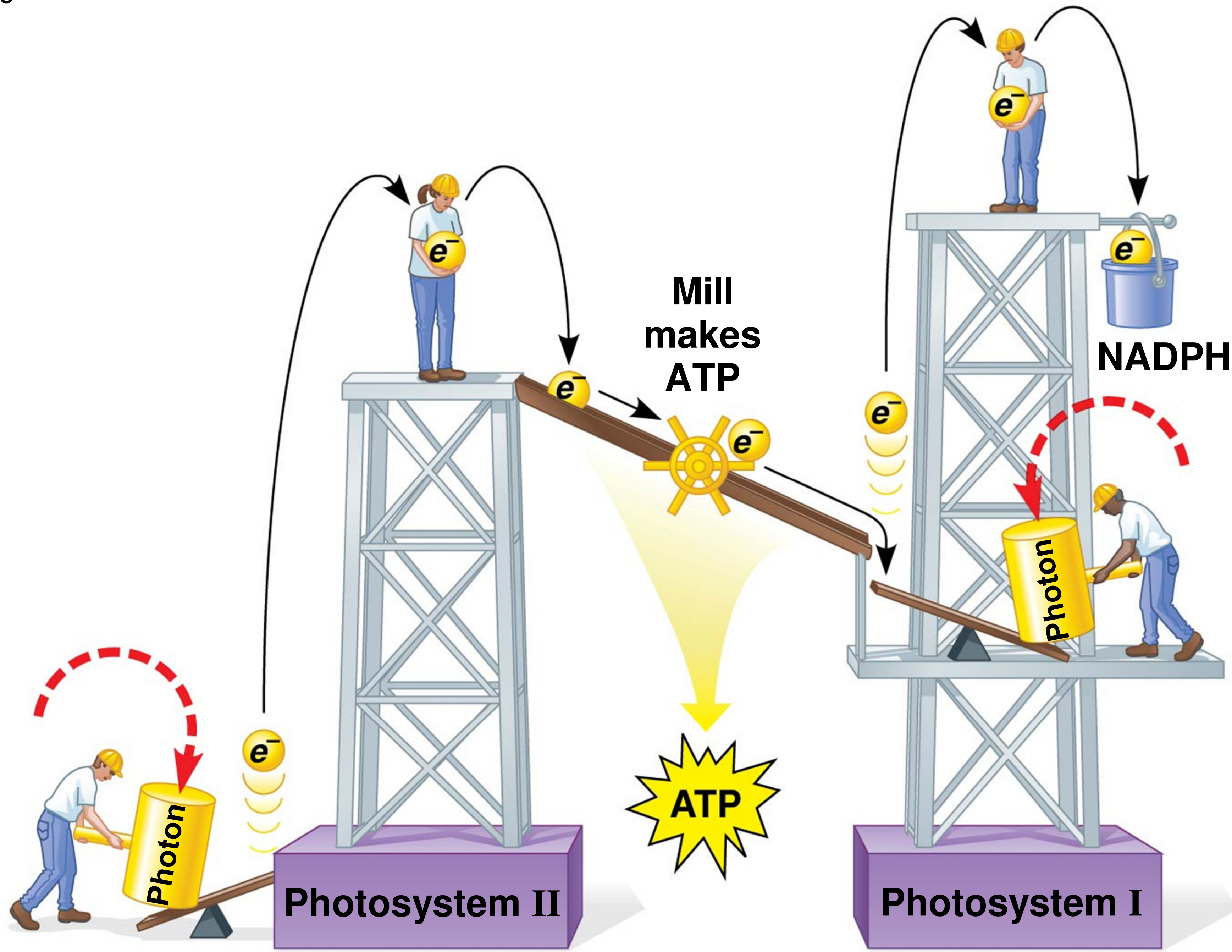
Light Reactions

- Chloroplasts are solar-powered chemical factories
- Their thylakoids transform light energy into the chemical energy of ATP and NADPH
- Leaves appear green because chlorophyll
  - Absorbs violet-blue and red light
  - Reflects and transmits green light

- Solar-powered transfer of an electron from a chlorophyll *a* molecule to the **primary electron acceptor** is the first step of the light reactions
- **Linear electron flow** involves the flow of electrons through two photosystems to produce ATP and NADPH using light energy

- Light reactions use solar power to generate ATP and NADPH
  - Provides chemical energy and reducing power so Calvin cycle can synthesize carbohydrates
  - Oxygen is a by-product

Figure 8.14



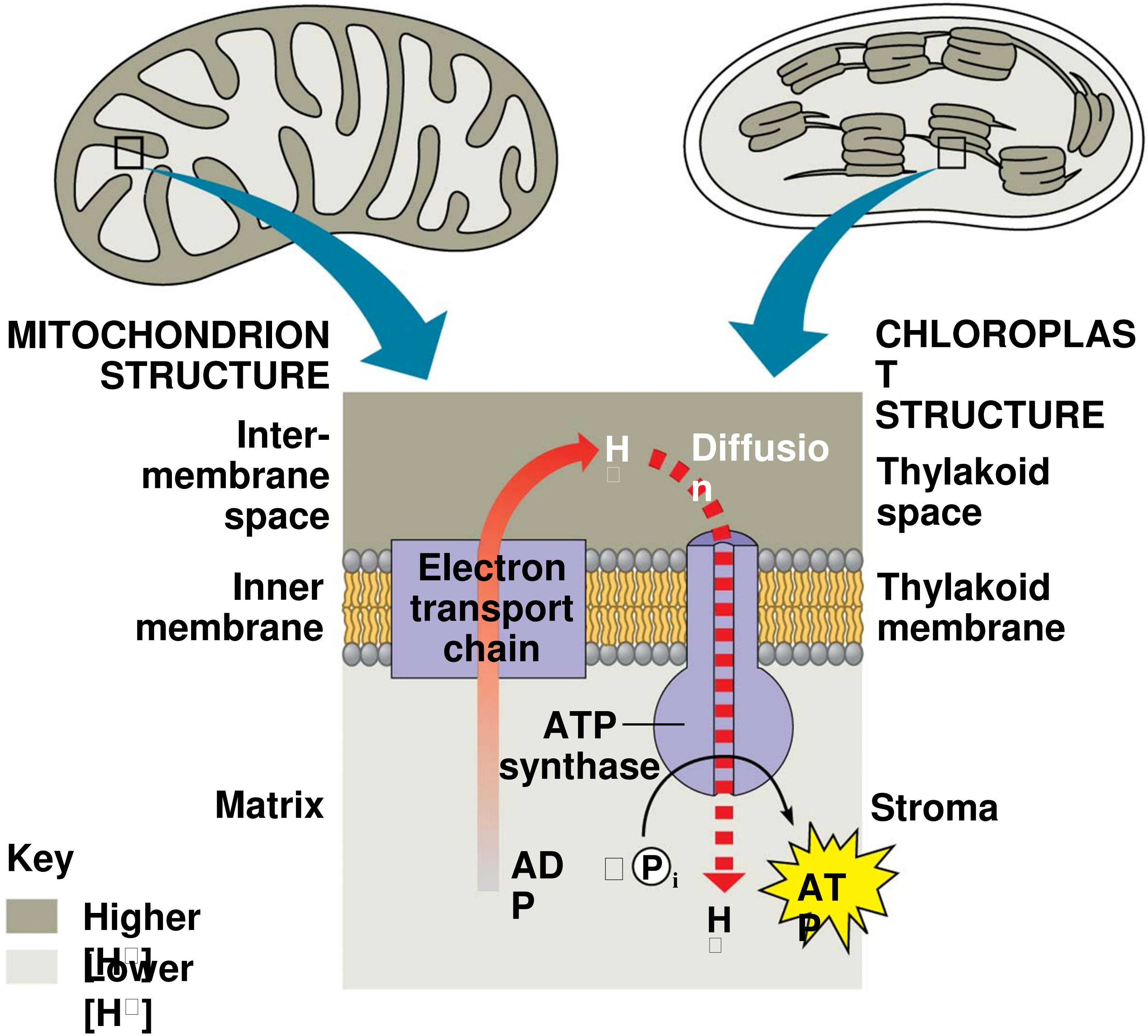
Mill makes ATP
NADPH
e⁻
Photon
ATP
Photosystem II
Photosystem I

A Comparison of Chemiosmosis in Chloroplasts and Mitochondria

- Chloroplasts and mitochondria both generate ATP by chemiosmosis but use different sources of energy
  - Mitochondria transfer chemical energy from food to ATP
  - Chloroplasts transform light energy into the chemical energy of ATP

- Spatial organization of chemiosmosis differs between chloroplasts and mitochondria but also shows similarities
  - Thylakoid space and intermembrane space are comparable
  - Mitochondrial matrix is analogous to stroma of chloroplast
- In mitochondria, protons are pumped to the intermembrane space and drive ATP synthesis as they diffuse back into the mitochondrial matrix
- In chloroplasts, protons are pumped into the thylakoid space and drive ATP synthesis as they diffuse back into the stroma

Figure 8.15


MITOCHONDRION STRUCTURE
Inter-membrane space
Inner membrane
Matrix
CHLOROPLAST STRUCTURE
Thylakoid space
Thylakoid membrane
Stroma
Electron transport chain
ATP synthase
H
Diffusion
ADP
P
i
H
ATP
Key
Higher [H]
Lower [H]

Calvin Cycle

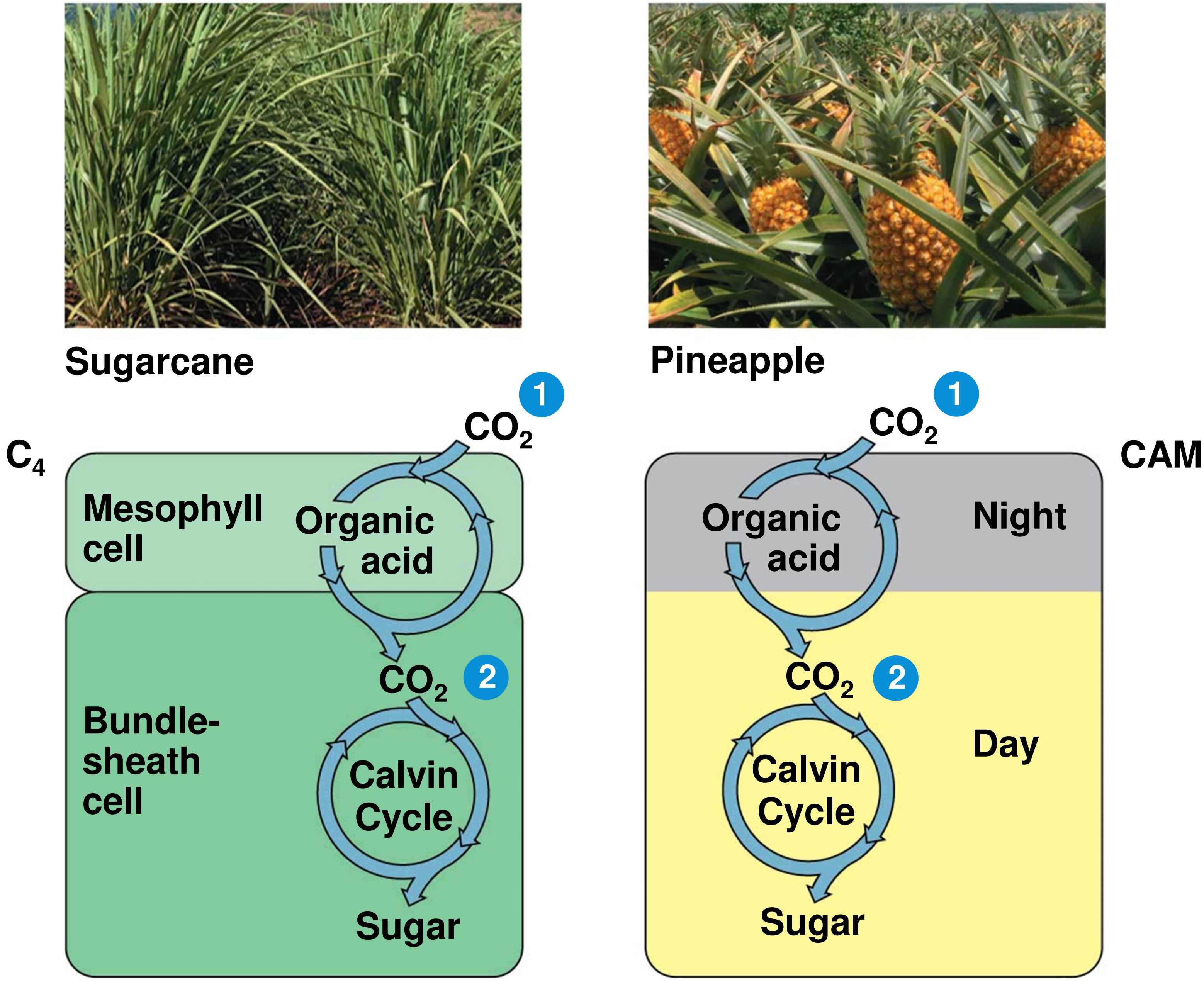
- Calvin Cycle uses the chemical energy of ATP and NADPH to reduce CO_2 to sugar
- Calvin cycle is anabolic
  - It builds sugar from smaller molecules
  - Consumes energy by using ATP and the reducing power of electrons carried by NADPH
- The Calvin cycle has three phases
  - Carbon fixation
  - Reduction
  - Regeneration of the CO_2 acceptor

Adaptations to prevent dehydration

- Stomata allows for exchange of gases but are also main avenues of evaporative loss of water
- On hot, dry days, plants close stomata, which conserves H_2O but also limits photosynthesis
  - This reduces access to CO_2 and causes O_2 to build up, leading to photorespiration
    - Uses ATP rather than generating it
    - Produces no sugar

- **C_4 plants**
  - Partially close stomata on hot/dry days to conserve water but sugar continues to be made
  - 2 different types of photosynthetic cells
    - Mesophyll cells
    - Bundle-sheath cells
  - Spatial separation of steps
- **CAM plants**
  - Close their stomata during the day and open them at night
  - Temporal separation of steps

Figure 8.18



(a) Spatial separation of steps

(b) Temporal separation of steps

Summary

- Light reactions
  - Occur in thylakoid membranes
  - Convert light energy to chemical energy of ATP and NADPH
  - Split H_2O and release O_2 to atmosphere
- Calvin Cycle reactions
  - Take place in stroma
  - Use ATP and NADPH to convert CO_2 to sugar
  - Return ADP and $NADP^+$ to light reactions